Posted
A & S
Off

GEORGIA INSTITUTE OF TECHNOLOGY
OFFICE OF RESEARCH ADMINISTRATION

RESEARCH PROJECT INITIATION

Date: June 12, 1975

Project Title: Organometallic Compounds of the Main Group Elements

Project No: G-33-603

Principal Investigator Dr. E. C. Ashby

Sponsor: National Science Foundation

Agreement Period: From June 1, 1975 Until November 30, 1976*
*12 months budget period plus 6 months for submission of required reports, etc.

Type Agreement: Grant CHE 75-04127

Amount: $33,000 - NSF Funds (G-33-603)
8,271 GIT Contrib. (G-33-366)
$41,271 Total

Reports Required:
Annual Letter Technical; Final Report

Sponsor Contact Person (s):

Administrative Matters
Mr. P. G. Naughton
Grants Mangger, Area 4
National Science Foundation
Washington, D. C. 20550
Phone: (202) 632-5965

Technical Matters
Dr. Christopher J. Michejda
Assistant Director - Chemical Dynamics Program
Chemistry Section
Division of Mathematical & Physical Sciences
National Science Foundation
Washington, D. C. 20550

Assigned to: School of Chemistry

COPIES TO:

Principal Investigator	Library
School Director	Rich Electronic Computer Center
Dean of the College	Photographic Laboratory
Director, Research Administration	Project File
Director, Financial Affairs (2)	
Security-Reports-Property Office ✓	
Patent Coordinator	Other

RA-3 (6-71)

Posted
Rec'd

GEORGIA INSTITUTE OF TECHNOLOGY
OFFICE OF CONTRACT ADMINISTRATION

SPONSORED PROJECT TERMINATION

Date: May 23, 1979

Project Title: Organometallic Compounds of the Main Group Elements

Project No: G-33-603

Project Director: Dr. E. C. Ashby

Sponsor: National Science Foundation

Effective Termination Date: 11/30/78 (Grant Expiration)

Clearance of Accounting Charges: by 11/30/78

Grant/Contract Closeout Actions Remaining:

- _ Final Invoice and Closing Documents
- X Final Fiscal Report via FCTR
- _ Final Report of Inventions
- _ Govt. Property Inventory & Related Certificate
- _ Classified Material Certificate
- _ Other _____

Assigned to: Chemistry (School/Laboratory)

COPIES TO:

- Project Director
- Division Chief (EES)
- School/Laboratory Director
- Dean/Director—EES
- Accounting Office
- Procurement Office
- Security Coordinator (OCA)
- Reports Coordinator (OCA)
- Library, Technical Reports Section
- Office of Computing Services
- Director, Physical Plant
- EES Information Office
- Project File (OCA)
- Project Code (GTRI)
- Other _____

CA—4 (3/76)

G-33-603

GEORGIA INSTITUTE OF TECHNOLOGY
ATLANTA, GEORGIA 30332

CHEMISTRY

January 18, 1977

Dr. Christopher J. Michejda
Assistant Program Director
Chemical Dynamics Program
Chemistry Section
Division of Mathematical & Physical Sciences
National Science Foundation
Washington D. C. 20550

Dear Dr. Michejda,

Thank you for your letter dated January 5, 1977. I am forwarding the following according to your request: (1) a brief technical report (plus papers published or submitted for publication) for the time period June 1, 1976 - May 31, 1977, (2) a budget for the time period June 1, 1977 - May 31, 1978, and (3) a statement of funds estimated to remain at the end of the present time period (June 1, 1976 - May 31, 1977).

Since this is the final year of our NSF grant, I plan to submit a revewal proposal by September 1, 1977 for possible support before our May 31, 1978 grant period ends.

Once again I would like to thank you for your help in arranging the many details for the grant.

Sincerely,

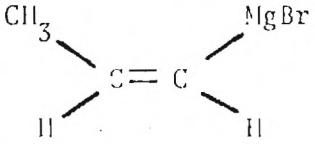
E. C. Ashby
Regents' Professor of Chemistry

Brief Technical Report (June 1, 1976 - May 31, 1977) NSF No. MPS7504127

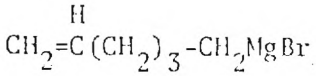
During the past report period one paper has appeared in the Journal of the American Chemical Society and three papers have been submitted for publication concerning the work carried out on the NSF program. In addition, we have presented the results of this work in the form of plenary lectures as well as submitted papers at regional ACS meetings. This past August the senior investigator served as Chairman of the Gordon Conference on Organometallic Chemistry.

Our major thrust has continued in the area of organometallic reaction mechanisms and composition of organometallic reagents in solution. With respect to the former we find ourselves in the middle of studies that are directed toward the exact description of alkyl transfer in organometallic addition reactions. This point is very important because it strikes at the very heart of the understanding of all main group organometallic reactions. Whether or not a reaction proceeds by a carbonionic mechanism or single electron transfer mechanism speaks not only to problems of mechanism, but stereochemistry, regioselectivity, etc. We have prepared the following probes in order to study this problem.

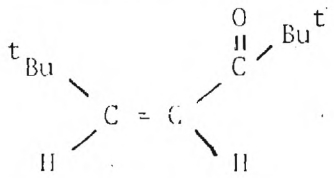
Organometallic Probe



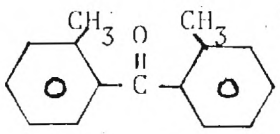
cis and trans



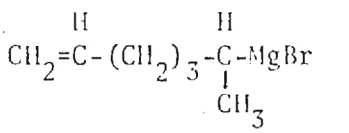
Substrate Probe

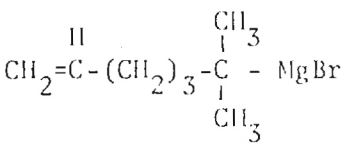


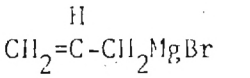
cis and trans

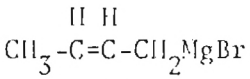


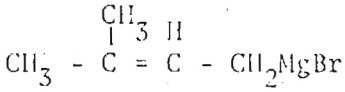
Organometallic Probe



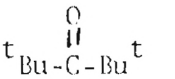




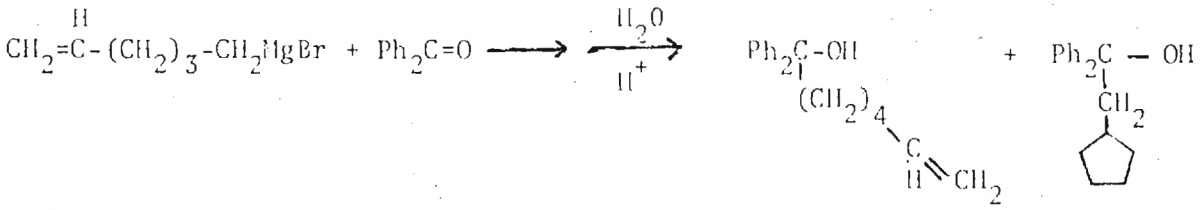




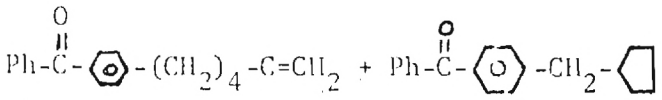
Substrate Probe



A typical reaction is the following:

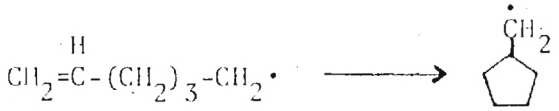


(A) (B)



(C) (D)

Since only product (A) is found in this reaction, it would appear that the reaction proceeds by a carbonionic mechanism or if by SET the radical is need free.



We have carried out a considerable amount of work in the area of composition of lithium alkyl cuprates in ether solvents and the resulting reactions of some of

the new cuprates that we have discovered (see preprints, enclosed).

In addition we have begun studies on the addition of HMgX compounds to olefins and alkynes. Our recent finding that we can prepare easily THF soluble HMgCl and HMgBr opens the way for investigating an alternate to the hydroboration reaction.

$$MgH_2 + MgCl_2 \longrightarrow HMgCl \xrightarrow{RC{=}CH_2} RCH_2CH_2MgCl$$

Since the C-Mg bond is much more versatile than the C-B bond and since HMgCl is considerable more economically attractive than B_2H_6, we feel that this reaction could hold great promise.

Statement of Current Support and Pending Proposals

1. We presently have a contract awarded by the Office of Naval Research for $42,000 for the time period April 1,1976 - March 31, 1977 entitled, "Chemistry of Complex Metal Hydrides". We have had this support for 9 consecutive years, but have just been informed that this year will be the final year of support. ONR will entertain a proposal for $15,000 for April 1, 1977 - March 31, 1978 to phase out the program completely.

2. We have just been awarded a grant of $24,000 for 3 years by the Petroleum Research Fund beginning September 1, 1977. The title of the grant is "An Evaluation of New and Unusual Simple and Complex Metal Hydrides of the Main Group Elements as Stereoselective and Regioselective Reducing Agents".

Estimate of Total Expenditures and Commitments on Grant NSF No. MPS7504127 and Funds Remaining at the End of the Current Report Period (May 31, 1977).

Personal Services	$32,050
Retirement	564
Material and Operating Expenses	11,192
Travel	400
Total Direct Costs	$44,206
Overhead (68% of salaries)	21,794
Total Amount of Grant	$66,000
Projected Residual Balance	-0-

G-33-603

NATIONAL SCIENCE FOUNDATION
Washington, D.C. 20550

FINAL PROJECT REPORT
NSF FORM 98A

PLEASE READ INSTRUCTIONS ON REVERSE BEFORE COMPLETING

PART I–PROJECT IDENTIFICATION INFORMATION

1. Institution and Address	2. NSF Program	3. NSF Award Number
Georgia Institute of Technology Atlanta, Georgia 30332	Chemical Dynamics	CHE 7504127
	4. Award Period From 6/1/75 To 11/30/78	5. Cumulative Award Amount $99,000

6. Project Title: Organometallic Chemistry of the Main Group Elements: Mechanisms, Stereochemistry and Transition Metal Catalysis.

PART II–SUMMARY OF COMPLETED PROJECT *(FOR PUBLIC USE)*

The primary objectives of our work supported by NSF fall into seven catagories: (1) the determination of the detailed mechanism of Grignard compound addition to ketones; (2) the investigation of MgH_2 and its derivatives (HMgX, where X = OR, NR_2, halogen, alkyl and aryl) as selective reducing agents toward reducible organic substrates; (3) the investigation of MgH_2, $LiAlH_4$ and other main group metal hydrides, as hydrometallation agents; (4) the investigation of the pyrolysis of CH_3MgNR_2 and CH_3MgOR compounds as routes to primary amines and olefins, respectively; (5) the effect of transition metal catalysis on the reactions of Grignard reagents; (6) the validity of the concept of "product development control" and (7) the investigation of new "ate" complexes of copper in organic synthesis.

We have essentially been able to determine in some detail the mechanism of Grignard compound addition to ketones particularly with respect to the nature of alkyl transfer. We have also found HMgX compounds to be excellent stereoselective reducing agents and hydrometallation agents. We have also found an entirely new and potentially very attractive method for the dehydration of alcohols and conversion of 2° amines to 1° amines. Our recent finding that several "ate" complexes of copper exist, has led to an uncovering of the different reactivities of these compounds compared to $LiCuR_2$ compounds, and finally, it has been conclusively shown that "product development control" is not important in reductions involving $LiAlH_4$

PART III–TECHNICAL INFORMATION *(FOR PROGRAM MANAGEMENT USES)*

1. ITEM *(Check appropriate blocks)*	NONE	ATTACHED	PREVIOUSLY FURNISHED	TO BE FURNISHED SEPARATELY TO PROGRAM	
				Check (√)	Approx. Date
a. Abstracts of Theses		X			
b. Publication Citations		X			
c. Data on Scientific Collaborators					
d. Information on Inventions					
e. Technical Description of Project and Results					
f. Other *(specify)*					

2. Principal Investigator/Project Director Name *(Typed)*	3. Principal Investigator/Project Director Signature	4. Date
E. C. Ashby		5/14/79

NSF Form 98A (5-78) Supersedes All Previous Editions

Form Approved OMB No. 99R0013

ABSTRACTS OF THESES

Joseph S. Bowers, Jr.

S. A. Noding

J. J. Lin

T. L. Wiesemann

G. F. Willard

J. S. Bowers, Jr.

BOWERS, Joseph Stanton, Jr., Ph.D. Georgia Institute of Technology, 1978. 120pp. Director: Dr. E. C. Ashby

The formation of "CH_3MgBr" from magnesium and methyl bromide in ether has been shown to be accompanied by the formation of about 0.2% of a very reactive magnesium hydride species. This hydride has been shown to be responsible for the formation of benzhydrol in reactions of benzophenones using a large excess of "CH_3MgBr". The relationship between the grade of magnesium used to prepare the Grignard reagent and the amount of 2-methylbenzhydrol formed was determined to be due solely to the size of the magnesium turnings and to the rate at which methyl bromide was added to the magnesium. Excess methyl bromide has been shown to destroy the activity of this hydride.

Radical probes were incorporated into the R-group of Grignard reagents such that radical character could be observed as isomerization or cyclization of the particular probe. Reactions between cis-propenylmagnesium bromide, 5-hexenylmagnesium chloride, 1,1-dimethyl-5-hexenylmagnesium chloride and 2,2-dimethyl-5-hexenylmagnesium chloride with benzophenone and 2-methylbenzophenone in diethyl ether, THF and n-butyl ether established that SET character was observable in the reactions of primary and tertiary Grignard reagents with benzophenone. Apparently an intermediate radical anion-radical cation pair is formed, which can collapse to give 1,2-addition product or dissociate to form a radical anion and a free radical within the solvent cage which in turn can collapse to 1,2-addition or conjugate addition (dependent upon radical reactivity, solvent, and steric factors) or escape the solvent cage to form pinacol.

Trialkylaluminum reagents were found to react with benzophenone via a polar mechanism evidenced by their transfer of 1° alkyl groups to benzophenone preferential to 3° alkyl groups.

Organolithium reagents appear to react through a SET mechanism with benzophenone by virtue of the similarity in the yield and product distribution shown by comparable Grignard and organolithium reactions with benzophenone.

SUMMARY

PART I. A STUDY OF STERIC APPROACH CONTROL VERSUS PRODUCT DEVELOPMENT CONTROL

The concept of "product development control" has been used to explain the stereochemistry of many reactions in which the observed isomer ratio reflects the stability of the product. This concept has been used particularly to explain predominant formation of the most stable isomer in reactions of $LiAlH_4$ and MeMgBr with substituted cyclohexanones. A study of the reaction of $LiAlH_4$ and MeMgBr with 7-norbornanone and its exo-2-methyl and endo-2-methyl derivatives shows that the most unstable isomer is formed exclusively and hence "product development control" is not a factor in these reactions. In an attempt to broaden the scope of this study, three series of reagents were studied: (1) $LiBH_4$, $LiAlH_4$ and $LiGaH_4$, (2) BH_3, AlH_3 and GaH_3, and (3) $(CH_3)_2Be$, $(CH_3)_2Zn$, $(CH_3)_2Mg$ and $(CH_3)_3Al$. In no case was "product development control" observed. The reactions with the 7-norbornanone system are similar in nature to those with cyclohexanones, except that the complicating factors of torsional strain, compression effects and conformational changes which are present in cyclohexanone systems are not present in the 7-norbornanone system. The concept of "product development control" is, therefore, a questionable one in ketone reductions involving $LiAlH_4$ and alkylations involving MeMgBr.

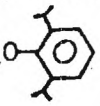
PART II. HYDROMETALLATION OF ALKENES AND ALKYNES CATALYZED BY TRANSITION METAL HALIDES

We have found that bis-dialkylaminoalanes, $HAl(NR_2)_2$, when allowed to react with alkenes or alkynes in the presence of a catalytic amount of Cp_2TiCl_2 provide high yields of deuterated or iodinated hydrocarbons when the reaction mixtures are quenched with D_2O or a benzene solution of iodine. These hydrometallated species were also allowed to react with carbonyl compounds (e.g. benzaldehyde); however, the normal addition products were produced in very low yields. Instead, associated tertiary amines ($PhCH_2NR_2$) were produced in substantial amounts. Our investigations also included other catalytic hydrometallation reactions of alkenes and alkynes with simple and complex metal hydrides. By using Cp_2TiCl_2 as a catalyst with $LiAlH_4$, $NaAlH_4$, Vitride, $LiAl(NEt_2)_2H_2$ and $NaAl(NEt_2)_2H_2$, $NaAl(NEt_2)_2H_2$, quantitative yields of deuterated products were obtained which in some cases were a distinct improvement over previous literature reports. Stoichiometric reactions of $LiH\text{-}VCl_3$ with ketones, aldehydes or enones were also investigated. Similar reactions with alkynes did not take place; however, with alkenes, the reactions produced alkanes although only a small amount of deuterium incorporation was observed when the reaction was quenched with D_2O.

A stereochemical study involving the reduction of cyclic ketones with $HCo(CO)_4$ was also undertaken. Unfortunately, the reactions were so slow that only small amounts of the corresponding alcohols (equal ratios of axial and equatorial alcohols) were produced.

A preliminary investigation of carbonylation of simple and complex metal hydrides in the presence of transition metal halide catalysts was also conducted. During this study no alcohol or formate products were observed.

PART III. REACTIONS OF MAGNESIUM HYDRIDE: STEREOSELECTIVE REDUCTION OF CYCLIC AND BICYCLIC KETONES BY LITHIUM ALKOXYMAGNESIUM HYDRIDES

A series of lithium alkoxymagnesium hydrides, $LiMgH_2(OR)$, were prepared and allowed to reduce 4-t-butylcyclohexanone (I), 3,3,5-trimethylcyclohexanone (II), 2-methylcyclohexanone (III) and camphor (IV). It was found that very bulky secondary cyclic alkoxy groups such as 2,2,6,6-tetramethyl- or benzylcyclohexoxy were very stereoselective in the reduction of these ketones. For example, $LiMgH_2$(O- ) reduced ketone (I) to provide 89% of the axial alcohol compared to HMgO-  which provided 83% of the axial alcohol.

The $LiMgH(OR)_2$ when R =  or  reagents were also found to reduce ketones (I), (II), (III) and (IV) stereoselectively but to a lesser extent and with more enolization than observed for the $LiMgH_2(OR)$ reagents.

PART IV : CONCERNING SALT EFFECTS ON THE STEREOSELECTIVITY OF ORGANOMETALLIC COMPOUND ADDITION TO KETONES

The reaction of 4-t-butylcyclohexanone with methyllithium in the presence of $LiClO_4$ resulted in the formation of the corresponding axial alcohol in 92% yield. This was a very unusual stereochemical observation in that only 65% of the axial alcohol was formed in the absence of $LiClO_4$. This result was attributed to complexation of the ketone by $LiClO_4$ followed by the addition of CH_3Li to the carbonyl group rather than by addition of a CH_3Li-$LiClO_4$ complex directly to the uncomplexed ketone. To complete a more detailed investigation of this unusual result, other salts and ketones were studied in a similar manner. In addition to CH_3Li, $(CH_3)_2Mg$ and $(CH_3)_3Al$ were also allowed to react with 4-t-butyl-cyclohexanone in the presence of equalmolar ratios of various salts were studied to exam the effect on the stereochemistry of the alcohol products.

It was shown that of all the salts tested, $LiClO_4$ had the greatest effect towards increased stereoselectivity of CH_3Li reagents. The other RLi reagents, t-butyllithium and phenyllithium, did not show as great an effect. Also, $(CH_3)_2Mg$ and $(CH_3)_3Al$ showed very little increased stereo-selectivity when allowed to react with ketones in the presence of metal salts.

PART V: ALKYLATIONS OF ENONES AND KETONES USING SUBSTITUTED ALKYLALUMINUM COMPOUNDS

Earlier workers in this group have shown that H_2AlI provided 100% of the 1,4-conjugate addition product when allowed to react with enones. The possibility of using R_nAlX_{3-n} compounds to promote the non-catalyzed 1,4-conjugate addition to enones under consistent conditions was studied. It was shown that for the enone reactions, the reagent which produced the greatest amount of 1,4-conjugate addition product without the presence of a catalyst was R_2AlI; however, the yield was low.

A systematic study concerning these compounds towards the alkylation of model ketone systems in order to find an effective stereoselectivity reagent was also investigated. It was observed once again that the most stereoselectivity reagent was R_2AlI, but the reaction was extremely slow. Therefore, it can be concluded that the use of these reagents to effect 1,4-conjugate addition of enones or stereoselectivity addition to ketones is impractical.

SUMMARY

PART I. THE EVALUATION OF HYDRIDE REAGENTS FOR CONJUGATE REDUCTION OF ENONES

Conjugate reduction of six enones by the new reagent $LiAlH_4$-CuI has been studied. The optimum conditions for conjugate reduction depend on the ratio of $LiAlH_4$:CuI:enone, temperature, solvent, and reaction time involving contact of $LiAlH_4$ and CuI before the enone is added. Enone I (see Table 1) can be reduced in quantitative yield and 100% regioselectivity in 1 hr or less when the ratio of $LiAlH_4$:CuI:enone is 1:4:1, the solvent is THF and the temperature is 0°. Enones II-VI (see Table 1) can also be reduced in high yield and 100% regioselectivity. Reduction of enones I and III with $LiAlH_4$-$TiCl_3$ proceeds with 100% regioselectivity, however the yields are lower (66 and 34%, respectively) compared with the results obtained with the $LiAlH_4$-CuI reagent. The reagent $LiAlH_4$-$FeCl_3$ was found to be ineffective for conjugate reduction. The new reagents, $LiAlH_4$-CuI and $LiAlH_4$-$TiCl_3$, show different stereoselectivity than $LiAlH_4$ toward 4-tert-Butylcyclohexanone and 3,3,5-trimethylcyclohexanone. Compared with $LiAlH_4$-CuI, related reagents ($LiAlH_4$-CuCl, $LiAlH_4$-HgI_2 and $LiAlH_4$-$HgCl_2$) show less regioselectivity in enone reduction, however, the reagent AlH_3-CuI is as effective in conjugate reduction as $LiAlH_4$-CuI. H_2AlI has been found to be the reactive species of the reagents $LiAlH_4$-CuI and AlH_3-CuI. The compounds H_2AlX and $HAlX_2$ where X = I, Br and Cl were synthesized independently

and were evaluated as conjugate reducing agents.

$HAl(O\underline{t}\text{-}Bu)_2$, $HAl(O\underline{i}\text{-}Pr)_2$ and $HAl[N(\underline{i}\text{-}Pr)_2]_2$ have also been found to be effective conjugate reducing agents. The alane, $HAl[N(\underline{i}\text{-}Pr)_2]_2$ in particular produced from the enones studies the 1,4-reduction product in quantitative yield and 99.5% regioselectivity. A six-center transition state for reduction was proposed.

PART II. REACTIONS OF NEW ORGANOCUPRATES

(II-1) Regioselective Methylation of Enones

The new organocuprates, $LiCu_2(CH_3)_3$, $Li_2Cu(CH_3)_3$ and $Li_2Cu_3(CH_3)_5$ were allowed to react with six representative enones in ether and THF in order to evaluate their regioselectivity and reaction rate compared to $LiCu(CH_3)_2$. In general, $LiCu_2(CH_3)_3$ in THF gave 100% regioselectivity in effecting 1,4- addition although its rate of reaction was slightly less than that of $LiCu(CH_3)_2$. On the other hand, $Li_2Cu(CH_3)_3$ reacted more rapidly in ether than did $LiCu(CH_3)_2$ with the same enones; however, when the enones were sterically hindered by α,β or β,β substitution, a significant amount of 1,2-addition product was observed. In THF, $Li_2Cu(CH_3)_3$ behaved very much like $LiCu(CH_3)_2$ except toward β,β-disubstituted enones. In ether, $Li_2Cu_3(CH_3)_5$ gave 100% 1,4-addition in each case studied and reacted more rapidly than $LiCu(CH_3)_2$.

(II-2) Substitution Reactions of Alkyl-, Cycloalkyl- and Aryl Halides

The new cuprates $LiCu_2(CH_3)_3$, $Li_2Cu(CH_3)_3$ and $Li_2Cu_3(CH_3)_5$ in Et_2O and THF have been compared to $LiCu(CH_3)_2$ and CH_3Li in their substitution reaction toward alkyl-, cycloalkyl- and aryl halides (where halogen = I, Br, Cl, F). In most cases the new cuprate

$Li_2Cu(CH_3)_3$ was superior to all other reagents and in some cases the superiority was substantial.

(II-3) Concerning the Reaction of Organocuprates with 4-tert-Butylcyclohexanone

The previously reported unusual stereochemistry in the reaction of 4-tert-butylcyclohexanone with CH_3Li-$LiCu(CH_3)_2$ is attributed to complexation of the ketone by $LiCu(CH_3)_2$ followed by addition of CH_3Li to the carbonyl group rather than by addition of a CH_3Li-$LiCu(CH_3)_2$ complex, e.g. $Li_2Cu(CH_3)_3$ directly to the uncomplexed ketone.

PART III. APPLICATION OF COMPLEX METAL HYDRIDES OF COPPER IN ORGANIC REACTIONS

A series of stable complex metal hydrides of copper of composition $Li_nCuH_{(n+1)}$ (n=1 to 5), prepared by the reaction of $LiAlH_4$ with the corresponding lithium methylcuprates in diethyl ether, has been allowed to react with selected alkyl halides, enones, and cyclic ketones in both diethyl ether and THF. It has been shown that the different hydrides exhibit different reducing capabilities towards alkyl halides, different regioselectivities towards enones, and different stereoselectivities towards cyclic ketones. These data support the integrity of each hydride as a single compound rather than a physical mixture. Tetrahydrofuran soluble Li_4CuH_5 has been shown to be the most reactive of the complex metal hydrides of copper toward alkyl halides in that this hydride reduced 1-iodo-, 1-bromo-, and 1-chlorodecane in 100, 100 and 99% yields, respectively. The complex metal hydrides of copper reduce enones predominantly 1, 4 (Li_2CuH_3, 96%) or 1, 2 (Li_4CuH_5, 95%)

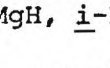
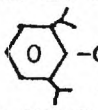
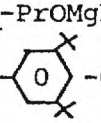
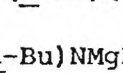
depending on the hydride. In most cases, the complex metal hydrides of copper reduce 4-tert-butylcyclohexanone predominantly from the axial side as in the case of $LiAlH_4$. Other cyclohexanones are reduced by the complex metal hydrides of copper similarly to $LiAlH_4$ except with less selectivity.

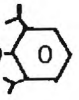
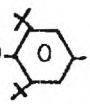
PART IV. FUNCTIONAL GROUP SELECTIVITY AND STEREOSELECTIVITY INVOLVING MAGNESIUM-HYDROGEN COMPOUNDS

(IV-1) Functional Group Selectivity

The reducing properties of magnesium hydride and 2,6-diisopropylphenoxymagnesium hydride have been demonstrated for the first time. The above hydrides have been shown to reduce benzaldehyde, 4-tert-butylcyclohexanone, 1-iodooctane, ethyl benzoate, benzoyl chloride, 2,2,6,6-tetramethyl-trans-4-hepten-3-one as well as other organic molecules with representative functionality. These hydrides have been found to be inert to 1-octene, phenylethyne, 1-bromodecane, 1-chlorodecane and iodobenzene.

(IV-2) Stereoselective Reduction

The stereochemistry of reduction of the representative ketones, 4-tert-butylcyclohexanone, 3,3,5-trimethylcyclohexanone, 2-methylcyclohexanone and camphor by magnesium hydride, alkoxyl magnesium hydrides (such as CH_3OMgH, i-PrOMgH, t-BuOMgH, Ph_3COMgH,  ,  ,  , and ), dialkylaminomagnesium hydrides (such as n-Pr_2NMgH, (i-Pr)(Me)NMgH, i-Pr_2NMgH, s-Bu_2NMgH,  ,  and (Me_3Si)(t-Bu)NMgH), and trihydridomagnesium derivatives

(such as H_3Mg_2O-  , H_3Mg_2O-  , H_3Mg_2O-  , H_3Mg_2OMe and $H_3Mg_2NPr_2^n$) has been determined. High stereoselectivity by some of the magnesium hydride derivatives was obtained and these results have been discussed.

PART V. REACTIONS OF LITHIUM ALUMINUM HYDRIDE-TRANSITION METAL HALIDES WITH ALKENES, ALKYNES AND ALKYL HALIDES

Admixtures of $LiAlH_4$ and first row transition metal chlorides were found to be excellent reagents for the reduction of alkenes, alkynes, and organohalides. The reactivity of the individual reagents varied depending on the metal halide. Eight alkenes, four alkynes, and twelve organohalides were involved in these studies. The results show that $LiAlH_4$ admixed with $FeCl_2$, $CoCl_2$, $NiCl_2$, and $TiCl_3$ are very promising reagents for the reduction of alkenes and halides. The reduction of alkynes to yield the alkenes or the alkanes depends on the metal halide, the ratio of reagent to substrate, the reaction temperature and the reaction time. $LiAlH_4$-$NiCl_2$ was found to be the best reagent to convert alkyne substrates to the corresponding alkenes selectively. A reduction mechanism involving cisaddition was observed.

PART VI. SELECTIVE REDUCTION OF ALKYNES BY MgH_2-CuI AND MgH_2-CuO-t-Bu

Five terminal and internal alkynes were allowed to react with the new reagents, MgH_2-CuI and MgH_2-CuO-t-Bu. The corresponding 1-alkene or cis-alkene was the only product observed for the reduction of terminal alkynes or internal alkynes, respectively.

SUMMARY

The reactions of methyl- and tert-butyl Grignard reagents with benzophenone, 2-methylbenzophenone (2-MBP), fluorenone and acetone were studied in an attempt to determine the influence of ketone reduction potential, solvent, magnesium metal purity and mode of Grignard preparation on the reaction mechanism.

The reaction of 2-MBP with methylmagnesium bromide was studied in detail. Methylmagnesium bromide prepared from magnesium samples containing significant amounts, ca. 20 ppm, of iron and other first row transition metals yielded substantial amounts of 2,2'-dimethylbenzopinacol at high Grignard to ketone ratios as well as normal addition products. Also, at low Grignard to ketone ratios, addition of catalytic amounts of iron and other first row transition metal salts to methylmagnesium bromide yielded large amounts of 2,2'-dimethylbenzopinacol. Multiple regression and correlation analysis shows a direct relationship between the amount of transition metal salt added to the Grignard reagent and the amount of pinacol formed. In reactions with 2-MBP, both erythro and threo pinacols were formed. The threo pinacol (isolated in substantial yield early in the reaction at low temperature) was shown to be the kinetic product which quickly converts to the thermodynamic erythro pinacol (95:5) at room temperature. A mechanism describing the transition metal catalyzed formation of pinacols is presented which is consistent with the known facts about this reaction. The formation of 2-methylbenzhydrol at high

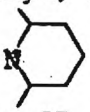
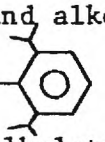
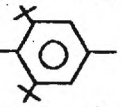
Grignard to ketone ratios was found to be due to a minor amount, ca. 0.2% of a very reactive magnesium hydride species formed during the reaction of methylbromide with magnesium metal in diethyl ether. The relationship between the grade of magnesium used to prepare the Grignard reagent and the amount of 2-methylbenzhydrol formed was found to be due solely to the size of the magnesium crystals or turnings and the rate at which methylbromide was added to the magnesium.

The reactions of methyl, tert-butyl and allyl Grignard reagents with cis- and trans-2,2,6,6-tetramethylhept-4-ene-3-one ("cis- and trans-enone") were studied to further investigate the extent of single electron transfer (SET) in Grignard reactions in the absence of transition metal impurities. It appears that the reaction with t-butyl Grignard reagents is predominantly SET, while the reaction with allyl Grignard reagents is predominantly polar. The mechanism involved in the "enone" reaction with methyl Grignard reagents is questionable, but most of the evidence favors a polar more than a SET pathway. In light of the various possible situations which may be encountered in the "cis-enone" probe system, however, there is an alternate explanation. All of the reactions may occur via a SET pathway to give a radical cation-radical anion pair. In the case of "t-BuMgCl", collapse of this pair to give products must be slower than isomerization of the "cis-ketyl" to the trans isomer. In the case of "Allyl MgBr" the opposite must be true: collapse to give products must be faster than isomerization. In methyl Grignard reactions with "cis-enone", collapse of the ion pair to give products must be comparable in rate to ketyl isomerization. Similar arguments could be made for the reactions of Grignard reagents with aromatic ketones.

The formation of pinacol in Grignard reactions with benzophenones, and the isomerization of starting enone in Grignard reactions with "cis-enone" have been shown to be inhibited by the presence of 20-30% p-dinitrobenzene in most cases. This information was used to further investigate the mechanism involved in the 1,2-addition of methyl Grignard reagents to ketones.

SUMMARY

PART I. STEREOSELECTIVE ALKYLATION OF CYCLIC KETONES BY DIALKYLAMINO AND ALKOXY (METHYL) MAGNESIUM COMPOUNDS

Dialkylamino (methyl) magnesium compounds, CH_3MgNR_2 (where NR_2 = NPr^i_2, NPh_2, and ), and alkoxy (methyl) magnesium compounds, CH_3MgOR (where OR =  and ), have been evaluated as stereoselective alkylating reagents. Two cyclic ketones, 4-t-butylcyclohexanone and 2,2,6,6-tetramethyl-4-t-butylcyclohexanone, were employed as model substrates. Excellent stereochemical results were obtained with diisopropylamino (methyl) magnesium and 2,6-diisopropylphenoxy (methyl) magnesium. Equatorial attack to give axial alcohol could be increased by adding triphenylphosphine to complex the reagent. Changing the solvent from diethyl ether to diphenyl ether also gave increased yields of axial alcohol. These reagents have considerable potential as stereoselective alkylating agents, especially for nonenolizable substrates.

PART II. THERMAL DECOMPOSITION OF THE ALKOXIDES AND AMIDES OF MAGNESIUM, ZINC, AND ALUMINUM

The thermal decomposition of the alkoxides and amides of magnesium, zinc, and aluminum has been studied. Kinetic and stereochemical data indicated that a cyclic, unimolecular six-center transition state was involved. The products from the alkoxides

were a hydrocarbon, an olefin, and a metal oxide, and the products from the amides were a hydrocarbon, an olefin, and a residue with empirical formula $(MgNR')_x$. The decompsoition reaction occurred in a syn stereochemical fashion and showed a large negative entropy of activation. Non-isothermal kinetic data agreed with the isothermal kinetic data to within 20%.

The product $(MgNR')_3$ represented a new class of pseudo-aromatic compounds analogous to the borazines: N-substituted magnazines. Spectroscopic and colligative property data supported this conclusion.

III(b) Publications

1. E. C. Ashby, J. Nackashi and G. E. Parris, "Composition of Grignard Compounds. X. NMR, IR and Molecular Association Studies of Some Methyl Magnesium Alkoxides in Diethyl Ether Tetrahydrofuran and Benzene," J. Am. Chem. Soc., 97, 3162 (1975).

2. E. C. Ashby, Irene G. Lopp, and Jerry D. Huhler, "Organiometallic Reaction Mechanisms. XIII. Identification of the Ketyl Intermeidates Formed in Reactions of Grignard Reagents with Ketones," J. Am. Chem. Soc., 97, 4966 (1975).

3. E. C. Ashby and S. A. Noding, "Evidence Against Product Development Control as an Important Factor in the Reduction of Ketones by Simple and Complex Metal Hydrides," J. Am. Chem.Soc., 98, 2010 (1976).

4. E. C. Ashby, T. L. Wiesemann, J. S. Bowers, Jr., and J. T. Laemmle, "Concerning the Formation of Magnesium Hydride in the Preparation of Grignard Reagents. The Origin of 2-Methylbenzhydrol in the Reaction of Methylmagnesium Bromide with 2-Methylbenzophenone," Tetrahedron Letters, No. 1, 21 (1976).

5. E. C. Ashby, J. D. Buhler, I. G. Lopp, T. L. Wiesemann, J. S. Bowers, Jr., and J. T. Laemmle, "Organometallic Reaction Mechanisms. 14. Role of Transition Metal Catalysts in the Formation of ARomatic Pinacols and Hydrols During Gringard Reagent Addition to Ketones, " J. Am. Chem. Soc., 98, 6561 (1976).

6. E. C. Ashby and J. J. Lin, "Highly Regioselective Reagents for Conjugate Reduction of Enones, $HAl(Ot\text{-}Bu)_2$, $Hal(Oi\text{-}Pr)_2$, $HAl[N(i\text{-}Pr)_2]_2$ and HBI_2," Tetrahedron Letters, No. 43, 3863 (1976).

7. E. C. Ashby and R. Scott Smith, "Concerning the Mechanism of Trimethylaluminum Addition to Benzophenone," J. Org. Chem., 42, 425 (1977).

8. E. C. Ashby, J. J. Lin and A. B. Goel, "Preparation, Properties, and Applications of Some New Complex Metal Hydrides of Copper, $Li_nCu_mH_{(n+m)}$," Tetrahedron Letters, 42, 3695 (1977).

9. E. C. Ashby, A. B. Goel, and J. J. Lin, "The Preparation of THF Soluble ROMgH and $ROMg_2H_3$ Compounds and Their Unusual Stereoselectivity in the Reduction of Cyclohexanones," Tetrahedron Letters, 36, 3313 (1977).

10. E. C. Ashby and J. J. Lin, "Reduction of Alkenes, Alkynes and Halides by Lithium Aluminum Hydride-Transition Metal Chloride," Tetrahedron Letters, 51, 4481 (1977).

11. E. C. Ashby and Steve Noding, "Hydrometallaion of Alkenes and Alkynes by Bis-Diisopropylaminoalane Catalyzed by Cp_2TiCl_2," Tetrahedron Letters, 52, 479 (1977).

12. E. C. Ashby and J. S. Bowers, Jr., "The Nature of Alkyl Transfer in the Reaction of Grignard Reagents with Ketones," J. Am. Chem. Soc., 99, 8504 (1977).

III(b) Publications (continued)

13. E. C. Ashby and S. Noding, "Concerning the Significance of Product Development Control as an Important Factor in the Reduction and Alkylation of Model Ketone Systems," J. Org. Chem., 43, 264 (1977).

14. E. C. Ashby, J. J. Lin and John J. Watkins, "Reactions of Enones with the New Organocuprates, $Li(Cu_2(CH_3)_3$, $Li_2Cu_3(CH_3)_5$ and $Li_2Cu(CH_3)_3$," J. Org. Chem., 42, 1099 (1977).

15. E. C. Ashby, J. J. Lin and John J. Watkins, "Unusual Stereoselectivity observed in the Reaction of CH_3Li-$LiCu(CH_3)_2$ with 4-Tert-Butylcyclohexanone," Tetrahedron Letters, 20, 1709 (1977).

16. E. C. Ashby and J. J. Lin, "Reactions of New Organocuprates. 2. Substitution Reactions of Alkyl-, Cycloalkyl- and Aryl Halides with $LiCu_2(CH_3)_3$, $Li_2Cu(CH_3)_3$ and $Li_2Cu_3(CH_3)_5$," J. Org. Chem., 43, 2805 (1977).

17. E. C. Ashby, J. J. Lin and A. B. Goel, "Reactions of Complex Metal Hydrides of Copper with Alkyl Halides, Enones and Cyclic Ketones," J. Org. Chem., 43, 183 (1978).

18. E. C. Ashby and T. L. Wiesemann, "Organometallic Reaction Mechanisms. 15. Factors Influencing the Nature of Grignard Reactions with Ketones," J. Am. Chem. Soc., 100, 189 (1978).

19. E. C. Ashby and J. J. Lin, "Transition Metal Catalyzed Reactions of Lithium Aluminum Hydride with Alkyl- and Aryl Halides," J. Org Chem., 43, 1560 (1978).

20. E. C. Ashby, J. J. Lin and A. B. Goel, "Reactions of Magnesium Hydrides. 1. Reducation of Organic Functional Compounds by Magnesium Hydride and 2,6-Diisopropylphenoxymagnesium Hydride," J. Org. Chem., 43, 1557 (1978).

21. E.C. Ashby, J. J. Lin and A. B. Goel, "Reactions of Magnesium Hydrides. 2. Stereoselective Reduction of Cyclic and Bicyclic Ketones by Hydridomagnesium Alkoxides," J. Org. Chem., 43, 1560 (1978).

22. E. C. Ashby, J. J. Lin and A. B. Goel, "Reactions of Magnesium Hydrides. 3. Stereoselective Reduction of Cyclic and Bicyclic Ketones by Dialkylaminomagnesium Hydrides," J. Org. Chem., 43, 1546 (1978).

23. E. C. Ashby, J. J. Lin and A. B. Goel, "A Convenient Method for the Stereoselective Reduction of Alkynes to Alkenes by the New Reagents MgH_2-CuI and MgH_2-CuO-t-Bu," J. Org. Chem., 43, 757 (1978).

24. E. C. Ashby and T. Smith, "The Hydrometallation of Alkenes and Alkynes with Magnesium Hydride," JCS Chem. Comm., 30 (1978).